

DISEASES OF THE CARDIOVASCULAR SYSTEM (SURGICAL)¹

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Many recent developments in the field of cardiovascular surgery constitute truly brilliant achievements, and the intensive investigations and bold ingenuity characterizing some of the experimental endeavors in this area portend other contributions of equal, if not greater, importance. Indeed the growth and scope of these endeavors have been so progressive and broadened that it is manifestly impossible in a review of this nature to give more than a general idea of some of the more significant accomplishments and trends of development. For this reason, and owing to limitation of space, primary consideration has been given to certain developments in surgery of the heart and allied great vessels.

PATENT DUCTUS ARTERIOSUS

Occlusion of the uncomplicated patent ductus arteriosus is now generally accepted as the only rational treatment of this congenital anomaly. Since the risk of operation is now so low [in 1947 the mortality following operation in 643 collected cases was 4.9 per cent (1) and in a similarly collected series of 509 cases reported this year it was 1.9 per cent (2 to 5)], it is also the consensus of most observers that the procedure is advisable in all patients except those older than 25 to 30 years of age who show no progressive cardiac hypertrophy or incapacitation from the fistula. Operation is also indicated in those cases complicated by subacute bacterial endocarditis, but only after prolonged intensive penicillin therapy.

The only point about which there is some disagreement in the management of this problem is essentially technical in nature and concerns the best means of occlusion. In the early cases, obliteration of the ductus was attempted by some form of ligation "in continuity." It soon became apparent, however, that this procedure was not entirely satisfactory, for in about 10 to 20 per cent of cases closure was incomplete or the fistula recurred (1, 5). Despite various modifications of this technique, there still remained a small percentage of recurrences. For this reason, Gross (5) finally evolved the technique of complete division and suture of the ductus. This proved so thoroughly satisfactory in his hands that all forms of ligation were completely abandoned.

Because this procedure is technically more difficult to perform and consequently more hazardous to the patient, some have questioned the desira-

¹ This review covers the period from approximately July, 1947 to July, 1949.

bility of its routine performance. Even such an experienced vascular surgeon as Blalock (6) prefers not to section the ductus, believing that the technique he employs is effective in maintaining closure and subjects the patient to less danger of fatal hemorrhage. His technique consists of pursestring sutures of silk placed and tied at the extreme ends of the ductus between which two through-and-through mattress sutures of silk are placed and tied, and over these a ligature of umbilical tape is tied.

With increasing experience and with the development of special instruments to facilitate the procedure and to assure greater safety in its performance, the method of complete division and suture appears to be gaining favor (2 to 4, 7 to 9). This attitude has been much advanced by the ingenious clamp devised by Potts (4) for this purpose. Containing a row of fine teeth in the opposing jaws, it can be applied to the vessel without injury and without danger of slipping off, thus permitting nontraumatic and safe handling of the divided ends of the ductus. Another technical improvement has been suggested by Freeman and his associates (9) and by Jones (2) for diminishing the dangers of hemorrhage during division of the ductus. This appears to be particularly useful under certain conditions, such as in an extremely short, wide ductus and in older patients with less elastic and more friable vessels. It consists of control of the components of the shunt by a clamp or ligature on the pulmonary end of the ductus and the application of a Potts-Smith clamp on the aortic side which allows adequate flow of blood through the lumen of the aorta but completely occludes the ductus opening into the aorta. With both ends of the ductus thus securely occluded, it may be safely divided and sutured.

COARCTATION OF THE AORTA

Approximately five years have now elapsed since Blalock & Park (10) first proposed and demonstrated experimentally a method for treating coarctation. This consisted in shunting the blood beyond the point of stenosis by anastomosing the left subclavian artery to the distal end of the aorta after resection of the coarctation. A short time later Crafoord & Nylin (11) and Gross & Hufnagel (12) performed the first successful operations on humans, consisting of excision of the stenotic area and end-to-end anastomosis between the proximal and distal ends of the aorta. Sufficient experience has now accumulated to establish certain conclusions concerning this method of therapy and to point up others that demand further study.

Technically there is general agreement that the ideal procedure is excision and end-to-end anastomosis. Unfortunately, this is not always feasible because in some cases the constriction may be too long to permit approximation of the ends after its excision or it may arise too close to the left subclavian artery. These difficulties are further magnified in older patients by extensive atherosclerosis. Under these circumstances the method proposed by Blalock & Park (10) of using the left subclavian artery to shunt blood to the aorta distal to the coarctation has been employed (13 to 19) but this procedure

has not proved entirely satisfactory (20). On the basis of his analysis of the follow-up results in 18 cases in which this was done, Shapiro (20) concludes that this procedure will be abandoned because apparently it is not sufficiently effective in reducing the load to the upper part of the body and increasing the flow of blood to the lower half. This belief is supported by the physiologic studies on cardiovascular dynamics made before and after operation by Brown and his co-workers (21), who found that the degree of return of cardiovascular function toward the normal state was significantly greater following end-to-end anastomosis than after subclavian-aortic anastomosis. The solution to this problem appears to be in the recent investigations of Gross and his associates (22 to 24) on preserved arterial homografts. These observers showed experimentally that aortic segments removed from donor dogs, when preserved in a proper medium, would remain viable for as long as 35 to 40 days and could be successfully used as grafts in recipient dogs. On this basis Gross and his co-workers (22 to 24) have grafted segments of preserved human aorta in nine patients following excision of the coarcted area and at the time of their report the grafted areas were still patent from three to nine months after operation.

Other technical considerations have been concerned primarily with the development of instruments to facilitate the operative procedure (17, 25, 26). Of these the clamp devised by Potts (4) and discussed under the section dealing with patent ductus appears to be the most useful. For patients in whom the coarcted segment begins close to the origin of the subclavian artery, Blalock and his associates have devised a modified Potts-Smith clamp which occludes the aorta but permits some circulation through the subclavian during the period required for the anastomosis.

The development of a successful surgical attack on coarctation of the aorta has stimulated renewal of interest in the physiopathology of this interesting lesion. A number of investigators have applied various methods of study before and after corrective surgical procedures to provide a better understanding of the cardiovascular dynamics of these patients and to permit greater accuracy in the diagnosis and evaluation of operative therapy. Among the most significant of these studies are those reported by the group of investigators at the Mayo Clinic and at the Johns Hopkins University. With few exceptions, notably blood flow studies, their observations were essentially similar.

Using the venous occlusion plethysmograph with the compensating spirometer recorder, Wakim, Slaughter & Clagett (27) observed that the resting blood flow in the upper and lower extremities of these patients does not differ significantly from that of normal persons. These observations are in accord with those previously reported by Lewis (28). After corrective surgical treatment there was a slight average decrease of blood flow to the arms and a slight increase of flow to the legs. On the other hand, Bing and his associates (19) found that the blood flow through the forearm was significantly elevated above normal and that through the legs below normal,

whereas after operation these values returned toward normal. Owing to variation in technique these apparently conflicting observations are probably not comparable and further studies are required before final evaluation can be made.

Intra-arterial blood pressure determinations by means of the hypodermic strain gauge manometer showed that in the arm both the systolic and diastolic pressures were significantly elevated above normal, whereas in the leg the systolic pressure was below normal and the diastolic pressure above normal (21, 29). Somewhat similar observations were made by Bing and his associates (19) except that they noted little deviation from normal in the diastolic component in the femoral artery. Both groups of observers found that following corrective surgical treatment of the coarctation these alterations in arterial pressure tended to return toward normal.

Comparative studies of the pulse wave contours in the femoral and in the brachial (Hopkins) or radial arteries (Mayo), made by both groups of investigators, showed delayed onset of the femoral pulse wave with prolongation of the normal interval between the onset and attainment of the peak, and a broad, rounded peak and absence of the notch normally present on the descending limb, giving a characteristic "sawtooth" pattern. This configuration of the femoral pulse wave is attributed to the "damping" effect produced by the area of resistance at the aortic stricture. The fact that, following surgical removal of the coarcted segment and end-to-end anastomosis of the aorta the femoral pulse wave assumes a more normal contour, supports this explanation (21). Further support of this concept may be derived from the recently reported ballistocardiographic wave pattern, which shows a characteristic short J K stroke produced by early abrupt interruption of the flow of blood at the coarcted area. Following corrective surgical treatment of the coarctation a typically normal J K stroke was obtained (30). On the basis of these observations and calculations of peripheral vascular resistance Bing and his associates (19) came to the conclusion that the hypertension in coarctation is probably not attributable to a renal pressor mechanism but rather to the resistance presented by the stenosis and collaterals, as previously suggested by Blumgart and his co-workers (31).

AORTIC ARCH ANOMALIES

Considerable interest has been aroused recently in malformations of the aortic arch and its great vessels since the demonstration by Gross (32, 33) that disturbances resulting from compression of the trachea or the esophagus by such anomalies may be relieved by surgical therapy. The resulting increased awareness of the possible surgical significance of these anomalies has stimulated studies directed toward wider and more accurate clinical recognition of the problem and appropriate surgical measures for the various types of anomalies that may produce symptoms (34 to 37).

The development of proper roentgenographic techniques has now pro-

vided a fairly accurate means of determining the presence and nature of these vascular malformations (38 to 40). The numerous anatomic variations of these anomalies of the derivatives of the aortic arch system which may produce disturbances of the esophagus or trachea have been described and illustrated by Gross & Ware (41) and by Edwards (42). The former authors (41) classified them into three general types: (a) those with a right aortic arch with several variations; (b) those with a double aortic arch with one or both limbs patent, and (c) those with an anomalous right subclavian artery arising from the left side of the arch (*dysphagia lusoria*). Edwards (42) divided them into two groups depending upon whether the ductus arteriosus takes its origin from the left or right pulmonary artery. In his opinion the significance of this classification lies in the fact that surgical therapy in these anomalies is usually directed toward either the ductus or some structure that lies on the same side of the body as the ductus. Since the ductus usually lies on the same side as the upper portion of the descending aorta, visualization of this latter structure by roentgenography may be a helpful guide to the surgeon in determining the proper side on which to perform thoracotomy.

In general, surgical therapy in these vascular malformations consists of one of the following procedures, depending upon the type of anomaly encountered: (a) division of the anomalous subclavian artery; (b) division of the smaller or atretic (usually the anterior or left) limb of a double aortic arch; (c) division of the ductus (or *ligamentum arteriosus*), and (d) dislocation of an innominate or common carotid artery.

CONGENITAL PULMONIC STENOSIS OR ATRESIA AND TRANSPOSITION OF GREAT CARDIAC ARTERIES

For sheer brilliance of conception and technical execution the work of Blalock & Taussig (43 to 46) in devising a successful operative means of treating congenital malformations of the heart, in which there is an inadequate pulmonary blood flow, remains preeminent in the annals of cardiovascular surgery. Indeed, their considerations and observations on this subject, as presented in their original report in 1945, were so fundamental and thorough that all subsequent investigations have in large measure been merely confirmatory. To be sure, much additional information has been contributed to the problem through subsequent accumulation of extensive clinical experience and intensive physiologic studies. This has led to better understanding of the underlying physiologic disturbances, to greater knowledge of the anatomic variations encountered, to more accurate diagnostic methods and better selection of patients for application of treatment, and to modifications and improvement in technical procedures.

On the basis of their experience, Taussig (45) has succinctly presented the six criteria which have proved essential in the successful application of this method of therapy:

- (a) The primary difficulty must be lack of adequate pulmonary blood flow; (b)

there must be a pulmonary artery to which to anastomose the systemic artery; (c) a systemic artery must be available for the anastomosis; (d) the difference in pressure between the systemic and pulmonic circulations must be sufficiently great for blood to flow from the aorta to the lungs; (e) the structure of the lungs must be such that the patient can tolerate the collapse of one lung and the temporary occlusion of one pulmonary artery; and (f) the structure of the heart must be such that it can adjust to the altered circulation.

Taussig (46) further showed on the basis of this analysis that whereas malformations of the heart with pulmonary stenosis or atresia other than the tetralogy of Fallot are amenable to this method of surgical treatment, the operative risk is greater and the results are perhaps not as good in the former types as in the latter.

The underlying principle of this method of therapy consists essentially in the shunting of blood around the point of stenosis in the pulmonary artery by the creation of an artificial ductus arteriosus. This may be done by various operative procedures, most of which were enumerated in the original report of Blalock & Taussig (43). Experience has shown that when possible the preferable procedure is end-to-side anastomosis between the subclavian and pulmonary arteries (44, 47, 48). In this connection, Blalock (44) prefers the right subclavian branch of the innominate except in patients more than 12 years of age in whom the left subclavian is employed. The major technical modification of the operation was provided by Potts *et al.* (49) and Dammann *et al.* (50), who devised an ingenious clamp, which by partial occlusion of the aorta, permits blood to flow through it while side-to-side anastomosis to the pulmonary artery is being performed. Thus, with the use of this clamp the objections raised to this method by Blalock & Taussig, who included it in their original report among the possible operative procedures, were overcome. This method appears to have distinct advantages under certain circumstances (51), such as in patients in whom a systemic artery would be difficult or impossible to use. Since it permits adjustment of the size of the stoma, it is especially useful in infants or small children in whom the subclavian may be too small to furnish an adequate blood flow to the lungs. Finally, it avoids the dangers of cerebral damage which may follow the use of the carotid or innominate arteries.

Although great progress has been made recently in the surgical therapy of congenital heart disease, corrective procedures for many of these problems remain to be developed. Intensive efforts in the experimental laboratory, however, are being directed toward them. This is well exemplified by the recent report of Hanlon & Blalock (52) on their experimental observations on venous shunts as corrective procedures in complete transposition of the aorta and pulmonary artery. They were able to show that it is technically feasible to anastomose the pulmonary veins to the superior *vena cava* and thus transmit oxygenated blood to the right side of the heart, which offers a possible approach to the surgical treatment of complete transposition of the great cardiac arteries.

MITRAL STENOSIS

The impetus given cardiovascular surgery in recent years has produced a revival of interest in the surgical attack upon certain types of valvular disease (53 to 55), especially mitral stenosis (56 to 58), which lay comparatively dormant since the pioneering endeavors of Cutler and his associates (59, 60) and Allen & Graham (61) approximately twenty-five years ago. Efforts have also been directed toward both creation and closure of septal defects (62 to 64). The more recent attempts concerned with mitral stenosis may be classified into two general lines of approach, one indirect and the other direct. The former includes methods designed to by-pass the auricle and mitral valve or to relieve the associated pulmonary hypertension, and the latter is a direct surgical attack upon the stenotic valve.

Attempts to shunt blood from the pulmonary vein to the left ventricle through anastomosis of a venous graft have been made experimentally but such a by-pass has functioned for only a few days (65). It seems doubtful that this line of approach will be fruitful.

The other indirect approach to this problem, i.e., relief of the associated pulmonary hypertension, appears to offer greater possibilities, at least, in providing symptomatic relief from the recurring episodes of acute vascular crises within the lungs. This approach is based upon the well-known fact that in patients with mitral stenosis and atrial septal defects (Lutembacher's syndrome) acute pulmonary edema rarely develops, protection being afforded by the escape of blood through the atrial opening from the left auricle to the right auricle. On this basis Jarotsky (66) and O'Farrell (67) suggested that such a defect might be created surgically as a means of therapy. This procedure has been performed by both Harken (56) and Bailey (57, 58) on a few patients.

The obvious technical difficulties involved in such a procedure may have been overcome by the method recently devised by Blalock & Hanlon (64) and successfully carried out in experimental animals. With this technique an interatrial septal defect may be created under direct vision without interruption of the circulation, with minimal loss of blood and with fairly accurate control of size. The final benefits, however, to be derived from such a shunt remain open to question. Even though it be done only in patients with a normal cardiac output, as emphasized by Harken (56), the eventual effects of such a shunt may be deleterious as a consequence of reducing left ventricular output and of throwing an additional burden on the right ventricle.

Following this same line of reasoning, but with a view toward a less hazardous undertaking, Sweet (68) has produced an extracardiac shunt by making an anastomosis between the dorsal segmental branch of the right inferior pulmonary vein and the azygos vein. This procedure has the additional advantage that if it is subsequently determined that an excessive burden has been placed on the right side of the heart the shunt can be readily closed with little risk to the patient. Remarkable improvement following this procedure was reported by Bland & Sweet (68) in three of five patients,

satisfactory progress in one with insufficient time to warrant conclusion and death in one from severe recrudescence of rheumatic fever. Significant diminution of the abnormally high left intra-auricular pressure was observed following release of the shunt with no evidence of impairment in peripheral circulation. Like the foregoing procedure the theoretic merit of this 'procedure is also open to question. As emphasized by Swan (69), a "circus movement" of blood is created through the right ventricle throwing an additional burden on this side of the heart in the effort to maintain left ventricular output. It is possible that the consequent long term effects upon the heart would be deleterious but this is not yet known. Further observation and experience are essential for final evaluation but at present this method appears to offer some value at least in alleviating the serious episodes of acute vascular crises within the lungs.

Still another surgical approach designed to relieve the associated pulmonary hypertension by diminishing right ventricular output has been proposed by Cossio & Perianes (70). These observers attempted to achieve this objective by two procedures, ligation of the inferior *vena cava* below the renal veins and tricuspid valvulotomy, the latter being done by a specially devised instrument threaded through the internal jugular vein. After experimental observations with these methods, they were performed on patients with uncontrollable heart failure and pulmonary congestion. Of five patients in whom tricuspid valvulotomy was performed immediate improvement was reported in all but one, although only one patient survived as long as six months. Improvement was also reported following ligation of the *vena cava* but actual data on cases observed were not presented. The practical value of these procedures in mitral stenosis may be seriously questioned, for their lasting effect is obviously doubtful and their risk is admittedly high.

The various methods employed in the direct surgical attack upon the stenotic mitral valve include digital dilation, incision or excision and "valvuloplasty" or "commissurotomy." These procedures, with the possible exception of the latter ones, are generally similar to those previously attempted with results that are equally unimpressive. The terms, "valvuloplasty" and "commissurotomy," are employed by Harken (56) and Bailey (58) to designate the operative procedures which they have respectively described and which consist essentially in division of the fused valve leaflets at the commissures with the view of restoring some valvular action with minimal regurgitation. The essential difference between these two procedures seems to be that in the former the commissures are divided by a wedge-shaped resection, whereas in the latter this is done by simple incision. Insufficient time has elapsed to appraise these procedures adequately. Good immediate results have been reported by Bailey in four of seven cases and by Harken in one of two cases, all the others having had fatal termination.

Although at present these procedures appear to offer some promise in selected cases, it would seem that in addition to carrying a considerable risk

they are not essentially constructive procedures. For this reason research along the lines recently reported by Templeton & Gibbon (71) and directed toward reconstruction of cardiac valves under direct vision would seem to provide a more fruitful approach. Similarly the studies of Gibbon and his associates (72, 73), of Bjork (74), and of Jongbloed (75, 76) directed toward development of a method to provide extracorporeal circulation permitting exclusion of the heart and lung during the period required for intracardiac surgery, assume particular significance.

MYOCARDIAL ISCHEMIA

The surgical attack upon the problem of myocardial ischemia has been intensified in recent years, particularly in the experimental laboratory. In general, surgical efforts directed toward alleviation of angina pectoris and coronary sclerosis have taken two lines of approach: (a) interruption of the cardiosensory pain-conducting pathways with the possible simultaneous interruption of vasoconstrictor impulses, and (b) revascularization procedures designed to provide an additional source of blood to the myocardium.

The former method needs only brief consideration here, for its underlying anatomic and physiologic basis and its technical aspects have been fully discussed in earlier publications (77, 78). Interruption of the cardiosensory pathways is accomplished by chemical (alcohol) block or resection of the upper three or four thoracic sympathetic ganglia, or by posterior rhizotomy at corresponding levels. Choice of the proper surgical procedure depends upon the extent of cardiac involvement and the relative competency of the heart. In patients with sufficient cardiac reserve to tolerate the operation, ganglionectomy appears to be the procedure of choice (78, 79). The value of this method of surgical attack is essentially palliative, for there is no good evidence to show that myocardial function is significantly improved or life appreciably prolonged. For this purpose, however, and in light of the predominantly good results (75 to 85 per cent) and low risk (mortality of 10 per cent or less) in properly selected cases (77 to 80) the procedure seems warranted and probably deserves more extensive use.

The other surgical approach to this problem began with the pioneering experimental studies of Beck (81 to 83), who attempted to provide a new blood supply to the heart by grafting tissues onto the myocardium. Various tissues have been used as potential sources of new blood supply, both experimentally and clinically, by Beck as well as a number of subsequent investigators. These include the pectoral muscle, thoracic wall, pericardium and pericardial fat, omentum, lung, and internal mammary artery (81, 82, 84 to 90). Experimentally, it can be demonstrated that new vascular channels can be produced between the heart and these tissues and that this new blood supply can act as a protective measure against sudden complete occlusion of one of the coronary arteries. However, the duration, and the volume and direction of blood flow through this vascular granulation tissue have not been clearly established. More recently, another method proposed

for the relief of angina and improvement of the circulation to the heart consists of ligation of the coronary vein combined with pericoronary neurectomy (91, 92). Clinical evaluation of these methods is difficult, and in view of the high operative mortality [37.8 per cent (82, 83)] and their questionable efficacy, adoption of these surgical procedures has met with considerable reluctance.

The most recent and the most significant development in this field, if for no other reason than as a splendid technical achievement, has been the experimentally successful arterialization of the coronary sinus by Beck (93 to 96). This was accomplished in dogs first by anastomosis with the common carotid artery, and later by a free graft of vein between the aorta and the coronary sinus, the latter having been ligated at an earlier stage. This procedure was found to provide effective functional circulation to the heart as determined by critical ligation of a major coronary artery. Moreover, it was observed that it was possible by this procedure to deliver too much blood to the heart with fatal effects. According to Beck (96) "significant progress" has not yet been made in the clinical application of this procedure to humans. Of five patients operated upon two are living. As Beck himself points out, certain questions concerning this method remain unanswered. For example, to what extent is the arterial blood entering the venous system functionally active in providing oxygen-exchange to the tissue? Or how much of this arterial blood entering the coronary sinus by-passes the capillary bed entirely and escapes by communicating channels into the cardiac chambers? Under these circumstances would the effects of an arteriovenous fistula so close to the heart be deleterious? In addition, certain technical problems concerned with preventing thrombosis and maintaining patency apparently still offer some difficulties to be overcome (97 to 99). Finally, the question may be raised concerning the hazards of such a technically difficult procedure in patients with severe myocardial damage (97, 100). Although these and perhaps other questions require further study before the clinical usefulness of the procedure is established, it would seem that this is the most fertile approach to the problem yet developed.

HYPERTENSION

The most significant recent development in the surgical treatment of hypertension is concerned with the efforts to provide a critical evaluation of sympathectomy. To be sure, a number of procedures, which vary somewhat in detail, have been proposed with the objective of making the operation more extensive (101 to 105) but it seems doubtful that the beneficial results of these procedures will be significantly greater than those obtained by the more generally employed thoracolumbar operation (106, 107). The more important consideration is proper assessment of surgical therapy.

Complete and precise appraisal of the therapeutic role of sympathectomy in hypertension has been attended with much difficulty. To a great extent this may be explained by the fact that the cause of the disease remains ob-

scure. It may also be explained by variations in the character and prognosis of the disease. Moreover, there seems to be a wide variety of criteria and divergence of methods employed by different observers in assessing the beneficial effects of therapy. Finally, properly controlled study with rigorously comparable series of surgical and nonsurgical cases would be extremely difficult, if not impossible, to make. For these and other reasons the various attempts which have been made to evaluate surgical therapy are all open to question (105, 106, 108 to 117). Perhaps the best efforts of this kind are contained in the recent reports of Evelyn, Alexander & Cooper (118) and Keith, Woolf & Gilchrist (119).

On the basis of these observations as well as accumulated clinical experience, it seems possible now, in spite of the difficulties previously mentioned, to make certain statements concerning the benefits and limitations of sympathectomy in hypertension. (*a*) There is general agreement that fairly complete denervation of the splanchnic bed and lower half of the body is desirable; whether more extensive denervation is necessary and would provide greater benefits is a matter for further study. (*b*) Favorable effects, especially in subjective symptoms, can be obtained in a high proportion of cases, though due consideration must be taken of such factors as age, sex, character of the disease, and extent of the pathologic process. (*c*) The blood pressure can be significantly reduced in about a fifth to a fourth of all cases, even cases of malignant hypertension unresponsive to medical management, but the longer the patients are followed, the less favorable are the results. This is well illustrated by the reported analysis of Evelyn and co-workers (118) in which it was found that the percentage of favorable results two years after sympathectomy was 41, whereas five years after sympathectomy this figure had progressively decreased to 21. (*d*) In general, the best results are obtained in younger patients, preferably those under 45 years of age, with pronounced vasospastic elements and minimal evidences of organic changes. (*e*) The chances of a good result, at least in so far as mortality is concerned, seem to be somewhat better in women than in men. (*f*) Patients with unusually high diastolic pressures do not respond well if serious organic changes have occurred. (*g*) In patients with malignant hypertension which is not associated with severe renal or cardiac impairment, sympathectomy may offer the only hope of palliation. (*h*) Patients with the characteristic form of late benign hypertension and with clinical evidence of diffuse arteriolar disease obtain relatively little benefit from the operation. In the more moderate form of benign hypertension without severe associated cardiac or renal impairment, the operation seems to provide some benefits.

Although accumulated experiences and analyses of results have provided certain general ideas concerning selection of cases for operation, there are still, as Palmer (113) emphasizes, "no positive tests or categories by which success or failure may be predicted accurately in an individual patient." A drop in blood pressure to normal or near normal level following bed rest, sedation, spinal anesthesia or other procedures is a favorable but not a

positive sign; it is often observed in patients who subsequently obtain no enduring benefits from operation. According to deTakats & Fowler (108, 109), attempts to distinguish between what is known as neurogenic hypertension, in which sympathectomy might be indicated, and humoral or renal hypertension, in which it would not be, by means of preliminary testing with spinal anesthesia have not been satisfactory.

Finally, certain troublesome and even disabling effects of sympathectomy must be taken into consideration before the operation is performed and must be balanced against the ultimate result. The possibility of their occurrence may be the deciding factor in determining the operability in a given case. They consist essentially, as Palmer (113) has pointed out, in the frequent occurrence of pronounced orthostatic hypotension, neuritis or pain, especially in the back, and often girdle-like, and occasional annoying vasomotor, sudomotor and even visceromotor disturbances which are probably the result of the compensatory or unbalancing effects of the operation. Some of these disturbances may persist for weeks or months, and although most of them disappear in time or can be controlled, they are occasionally severe and disabling.

PERIPHERAL VASCULAR DISEASE

In the field of peripheral vascular disease there has been continued interest in the development of better means of investigation, improved methods of treatment, and more accurate evaluation of therapy. The importance of developing a simple and clinically practical method of measuring peripheral blood flow is generally recognized, for such observations are essential not only in providing better clinical management but also in permitting more accurate objective evaluation of different forms of therapy.

Among the more recent developments directed toward this objective are two methods of study utilizing radioactive substances. In one, blood flow measurement is based upon the "build-up" of radioactive sodium (Na^{24}) in the tissues of the extremities following its intravenous injection in the arm (120), whereas in the other it is based on the rate of disappearance of the intramuscularly injected radioactive sodium or its clearance from the tissues (121 to 123). Since several variables, including blood flow, diffusion, and variety of tissues concerned in the measurement are involved in the former method, its use as an accurate means of studying circulatory physiology of the extremities and peripheral vascular disturbance is open to question. For this purpose the second method appears to rest on sounder ground. But here again the rate of diffusion of sodium chloride is an important factor, since the rate of disappearance of the substance deposited in the extravascular spaces must depend not only upon the rate and volume of blood flow in the surrounding tissues but also upon the rate at which the radioactive substance crosses the membranes into the circulating blood and lymph. If it can be assumed that this rate of diffusion is constant under all circumstances of vascular disorders, this method of study can be expected to provide a good indication of the effective circulation of the part. Preliminary observations

by Elkin and his associates (122) and by Kety (121), who devised this method of study, suggest that it does provide a fairly accurate means of determining the clearance of a diffusible ion in tissues, and that this represents a valid quantitative measurement of the regional circulation. It seems, therefore, to offer another valuable aid in the objective evaluation of various forms of therapy in peripheral vascular disturbances and especially in their effect upon the deep circulation of the part.

In the therapy of peripheral vascular disturbances sympathectomy has assumed increasing significance as the most effective means of producing a maximum increase in the blood supply of a diseased part. The rationale of sympathectomy in peripheral vascular disease is the production of vasodilatation by interruption of the vasoconstrictor impulses transmitted over sympathetic pathways to the vascular bed. In the concept of hemodynamics, to which the term hemometakinesia has been applied, a further rational basis for sympathectomy is provided (124, 125). This concept is derived from certain observations concerning the physiology of the circulation which establish the presence of spontaneous and even rhythmic fluctuations in the volume of organs primarily attributable to changes in the volume of blood within the part. These fluctuations of the blood volume in different parts of the body can occur without any alteration in the total blood volume by an adjustment of the vascular bed which permits simultaneously an increase in the volume of blood (vasodilatation) of one part of the body and a corresponding decrease elsewhere (vasoconstriction). This, in effect, constitutes a compensatory mechanism permitting the "borrowing and lending" of blood by the various tissues to meet variations in requirements. It is indicative of a well regulated mechanism designed to permit the body to utilize its limited total blood volume in the most efficient manner. In this mechanism of control and regulation of the peripheral vascular bed, which provide adjustments in the volume of blood in the part, the sympathetic nervous system plays an important role. Interruption of the sympathetic pathways, to the part removes the vasoconstrictor factor in this mechanism and through the resultant maximum vasodilatation in the vascular bed provides an increase in the circulation of the part.

In the treatment of peripheral vascular disease, other means of producing such vasodilatation by the use of various vasodilator agents have long been attempted with little success. More recently with the development of more effective adrenolytic and sympatholytic drugs, such as tetraethylammonium chloride or bromide, dibenamine (dibenzylbetachlorethylaminohydrochloride and priscoline (2-benzyl 4, 5 imidazoline hydrochloride), some observers (126 to 129) have reported highly favorable results following the use of these agents in all types of peripheral vascular disturbances. Other investigators (124, 125, 130 to 132), however, have not been able to confirm these observations. Under controlled atmospheric conditions and using thermometric and plethysmographic methods of determining blood flow, Ray, Burch & DeBailey (124) observed that none of these vasodilator agents

could consistently produce, in a local peripheral part, vasodilatation equal either in degree or duration to that produced by sympathetic denervation of the part.

The indications and the value of sympathectomy in various forms of peripheral vascular disease have been recently reviewed by a number of observers (133 to 136). Although it is generally agreed that sympathectomy may be the most effective means of improving the circulation in many of these disturbances, it is also recognized that depending upon the type and extent of the disease, as well as on other factors, considerable variation exist in its efficacy. Much attention has been recently devoted to the factors which may alter or modify the enduring effectiveness of sympathectomy in peripheral vascular disturbances, particularly the phenomenon of return of vasomotor activity after sympathectomy. Extensive considerations of this problem with a critical evaluation of the factors involved have been presented in several recent reviews (107, 133, 134, 136 to 138). Among the most important factors concerned with this problem are local vascular faults, variable pathologic processes, increased responsiveness of denervated smooth muscles to circulating vasoconstrictor substances, regeneration or incomplete interruption of sympathetic pathways, recovery of intrinsic vascular tone, abolition of vasodilator influences, reorganization of neurogenic vasoconstrictor function within the sympathetic system, and residual sympathetic pathways (133). On the basis of present knowledge it is difficult to evaluate the relative importance of the role played by each of these factors in modifying or limiting the enduring effectiveness of sympathectomy. It is possible that depending upon the nature of the disturbance and the type of procedure performed each one of them singly or in combinations may be operative and further studies are needed to clarify the problem. As emphasized previously (133), however, although it is important to acknowledge and appreciate the significance of possible limiting factors of sympathectomy, it is equally important to recognize that they do not necessarily contraindicate the procedure or even greatly restrict its application. They are important in the critical evaluation of the operation, and they constitute special problems which still require solution.

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